Supplemental Table 1Online database search strategy¹.

#1

(dietary OR food OR bariatric surgery OR physical activity OR sports OR exercise) AND (weight loss OR "body weight" OR Obesity OR obese OR abdominal obesity OR adiposity OR "waist circumference" OR body mass index)

#2

("short chain fatty acids" OR "short-chain fatty acid" OR "volatile free fatty acids" OR butyrate OR propionate OR acetate OR formate OR "butyric acid" [Title/Abstract] OR "propionic acid" [Title/Abstract] OR "acetic acid" [Title/Abstract] OR "formic acid" [Title/Abstract] OR valeric acid" [Title/Abstract] OR blood OR serum OR circulation OR "systemic circulation" OR stool OR faecal OR feeal or urine)

#3

(Randomized controlled trial OR randomized clinical trial OR randomized trial OR controlled trial OR clinical trial OR intervention study OR crossover trial OR randomized controlled study OR clinical study OR randomized study OR controlled study OR "single-arm" OR "open-label") NOT (animals [mh] NOT humans [mh])

¹#1, #2, and #3- search string 1, 2, and 3 respectively.

²PubMed and Web of Science = #1 AND #2 AND #3.

³Cochrane= #1 AND #2. Only search strings #1 and #2 were used in Cochrane.

Supplemental Table 2 Evaluation of the risk of bias in randomized controlled trials¹.

	Assessment criteria (reasons)							
Study	Random	Allocation	Selective reporting	Blinding of	Blinding of	Incomplete	Other bias	Overall
(ref)	sequence	concealment		participants and	outcome	outcome data		bias
	generation			personnel	assessment			
Benassi-	Unclear	Unclear	High (data for changes in	High (no blinding)	Low	Unclear (no	High	High
Evans et	(Not	(not	SCFA concentrations were		(not done, but	comment on	(potential	
al. (1)	described)	described)	not shown, although it was		outcome not	drop-outs and	conflict of	
			reported hence cannot be		likely to be	reasons for drop-	interest on the	
			included in a meta-analysis)		influenced by	outs)	part of a co-	
					blinding)		author-Noakes)	
Brinkworth	Unclear	Unclear	Low	High (no blinding)	Low	Low (reasons for	Low	High
et al. (2)	(inadequate	(not	(data on all outcomes of		(not done, but	attrition in both	(no other bias	
	description	described)	interest were presented)		outcome not	intervention	detected)	
	"participants				likely to be	groups were		
	were randomly				influenced by	provided)		
Cont. of all	assigned")	Unclear	Y (1.4 11 4	II' 1 (11' 1')	blinding)	T	T (TT' . 1.
Gratz et al.	Unclear (Not	(not	Low (data on all outcomes of interest were presented)	High (no blinding)	Low (not done, but	Low (outcome was reported for	Low (no	High
(3)	described)	described)	of interest were presented)		outcome not	all study	apparent form of other bias)	
	described)	described)			likely to be	participants)	other bias)	
					influenced by	participants)		
					blinding)			
Russel et	Unclear	High (upon	Low (data on all outcomes	High (no blinding)	Low	Low (drop-out	Low (no other	High
al. (4)	(Not	entry into the	of interest were presented)	ingii (iio oiiiidiig)	(not done, but	was reported and	form of bias	111511
(1)	described)	study)	or merese were presented)		outcome not	not related to	detected)	
	,	J ,			likely to be	study protocol)	,	
					influenced)	7 1		
Salonen et	Unclear	Unclear (not	Low (data on all outcomes	High (no blinding)	Low	Low (drop-out	Low (no other	High
al. (5)	(Not	described)	of interest were presented)		(not done, but	was reported and	form of bias)	
	described)				outcome not	not related to		
					likely to be	study protocol)		
					influenced)			
Duncan et	Unclear	Unclear	Low (quote: "all collected	High (no blinding)	Low	Low (drop-out	Low (no other	High
al. (6)	(Not	("with the	samples were analyzed" and		(not done, but	was reported and	form of bias)	
	described)	order	all outcomes were reported)		outcome not	not related to		
		randomized			likely to be	study protocol)		
		between			influenced)			
		participants")						

¹ ref- reference; SCFA- short-chain fatty acid.

Supplemental Table 3 Evaluation of the risk of bias in non-randomized interventions¹.

	Assessment criteria (reasons)								
Study (ref)	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias due to measurement of outcomes	Bias in selection of the reported result	Overall bias	
Damms- Machado et al. (7)	Moderate risk (participant assignment to the dietary and surgical interventions was based on current evidence-based guidelines)	Low risk (Selected participants were part of a multicenter clinical trial)	Low (interventions were actively assigned)	Low (no apparent deviation)	Low (no attrition, SCFA concentrations were measured in all participants at baseline and 6 and 9 months postintervention)	Low (no blinding, but this is not likely to influence the outcome of interest, objective measurements)	Low (values of SCFA concentrations at all time-points were reported)	Moderate	
Dao et al. (8)	Low (participants received the same intervention- single group assignment; baseline dietary assessment was carried out before the start of the intervention)	No information (all three related publications only mentions 'participants were recruited without describing further the method of recruitment)	Low (interventions were actively assigned)	Low (no apparent deviation)	Low (only one dropped out for personal reasons)	Low (assessment of acetate not likely to have been influenced)	Moderate (only acetate concentration was reported graphically, although NMR was used for total SCFA analysis. This was attributed however to sensitivity of NMR in detecting other components of SCFA)	Moderate	
Patrone et al. (9)	Low (participants received the same intervention)	Low (participant eligibility criteria was predefined)	Low (interventions were actively assigned)	Low (no deviation)	Low (no attrition, SCFA concentrations were measured in all participants)	Low (assessment unlikely to have been influenced)	Low (all outcomes of interest were reported)	Low	

¹ ref- reference; SCFA- short-chain fatty acid.

Overall risk of bias judgment

The overall risk of bias judgement for randomized controlled trials was based on the criteria provided in the Cochrane risk of bias tool for randomized controlled trials (10);

- i. Low risk of bias low risk of bias for all key domains
- ii. Unclear risk of bias unclear risk of bias for one or more key domains
- iii. High risk of bias high risk of bias for one or more key domains

The overall risk of bias judgement for non-randomized interventions was based the criteria in the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) guidelines (11);

- i. Low risk of bias low risk of bias for all domains
- ii. Moderate risk of bias low or moderate risk of bias for all domains
- iii. Serious risk of bias serious risk of bias in at least one domain, but not at critical risk of bias in any domain
- iv. Critical risk of bias critical risk of bias in at least one of the domains
- v. No information lack of clear indication of a critical or serious risk of bias and also absence of information in at least one key domain

Supplemental Table 4 Full-text studies excluded from the review with reasons¹.

Reasons for exclusion					
No SCFA	Non-weight loss trials	No assessment of outcome of interest ²			
Study (ref)	Study (ref)	Study (ref)			
Gralka et al. (12)	Bottin et al. (13)	Stroeve et al. (14)			
Haufe et al. (15)	Canfora et al. (16)	Tremaroli et al. (17)			
Johnston et al. (18)	Daud et al. (19)	Zheng et al. (20)			
Kamphuis et al. (21)	Olli et al. (22)				
Khakimov et al. (23)	Patil et al. (24)				
Kunesova et al. (25)					
Lewis et al. (26)					
Meckling et al. (27)					
Remely et al. (28)					
Yang et al. (29)					

¹ref- reference; SCFA- short-chain fatty acid.

²No statistical assessment of changes in SCFA concentrations after the intervention was performed.

Supplemental References

- 1. Benassi-Evans B, Clifton P, Noakes M, Fenech M. High-protein/high red meat and high-carbohydrate weight-loss diets do not differ in their effect on faecal water genotoxicity tested by use of the WIL2-NS cell line and with other biomarkers of bowel health. Mutat Res 2010;703(2):130-6. doi: 10.1016/j.mrgentox.2010.08.009.
- 2. Brinkworth GD, Noakes M, Clifton PM, Bird AR. Comparative effects of very low-carbohydrate, high-fat and high-carbohydrate, low-fat weight-loss diets on bowel habit and faecal short-chain fatty acids and bacterial populations. Br J Nutr 2009;101(10):1493-502. doi: 10.1017/s0007114508094658.
- 3. Gratz SW, Hazim S, Richardson AJ, Scobbie L, Johnstone AM, Fyfe C, Holtrop G, Lobley GE, Russell WR. Dietary carbohydrate rather than protein intake drives colonic microbial fermentation during weight loss. Eur J Nutr 2018. doi: 10.1007/s00394-018-1629-x.
- 4. Russell WR, Gratz SW, Duncan SH, Holtrop G, Ince J, Scobbie L, Duncan G, Johnstone AM, Lobley GE, Wallace RJ, et al. High-protein, reduced-carbohydrate weight-loss diets promote metabolite profiles likely to be detrimental to colonic health. Am J Clin Nutr 2011;93(5):1062-72. doi: 10.3945/ajcn.110.002188.
- 5. Salonen A, Lahti L, Salojarvi J, Holtrop G, Korpela K, Duncan SH, Date P, Farquharson F, Johnstone AM, Lobley GE, et al. Impact of diet and individual variation on intestinal microbiota composition and fermentation products in obese men. ISME J 2014;8(11):2218-30. doi: 10.1038/ismej.2014.63.
- 6. Duncan SH, Belenguer A, Holtrop G, Johnstone AM, Flint HJ, Lobley GE. Reduced dietary intake of carbohydrates by obese subjects results in decreased concentrations of butyrate and butyrate-producing bacteria in feces. Appl Environ Microbiol 2007;73(4):1073-8. doi: 10.1128/aem.02340-06.
- 7. Damms-Machado A, Mitra S, Schollenberger AE, Kramer KM, Meile T, Konigsrainer A, Huson DH, Bischoff SC. Effects of surgical and dietary weight loss therapy for obesity on gut microbiota composition and nutrient absorption. Biomed Res Int 2015;2015:806248. doi: 10.1155/2015/806248.
- 8. Dao MC, Everard A, Aron-Wisnewsky J, Sokolovska N, Prifti E, Verger EO, Kayser BD, Levenez F, Chilloux J, Hoyles L, et al. Akkermansia muciniphila and improved metabolic health during a dietary intervention in obesity: relationship with gut microbiome richness and ecology. Gut 2016;65(3):426-36. doi: 10.1136/gutjnl-2014-308778.
- 9. Patrone V, Vajana E, Minuti A, Callegari ML, Federico A, Loguercio C, Dallio M, Tolone S, Docimo L, Morelli L. Postoperative Changes in Fecal Bacterial Communities and Fermentation Products in Obese Patients Undergoing Bilio-Intestinal Bypass. Front Microbiol 2016;7:200. doi: 10.3389/fmicb.2016.00200.
- 10. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928. doi: 10.1136/bmj.d5928.
- 11. Sterne JA, Hernan MA, Reeves BC, Savovic J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ 2016;355:i4919. doi: 10.1136/bmj.i4919.
- 12. Gralka E, Luchinat C, Tenori L, Ernst B, Thurnheer M, Schultes B. Metabolomic fingerprint of severe obesity is dynamically affected by bariatric surgery in a procedure-dependent manner. Am J Clin Nutr 2015;102(6):1313-22. doi: 10.3945/ajcn.115.110536.
- 13. Bottin JH, Swann JR, Cropp E, Chambers ES, Ford HE, Ghatei MA, Frost GS. Mycoprotein reduces energy intake and postprandial insulin release without altering glucagon-like peptide-1 and

- peptide tyrosine-tyrosine concentrations in healthy overweight and obese adults: a randomised-controlled trial. Br J Nutr 2016;116(2):360-74. doi: 10.1017/s0007114516001872.
- 14. Stroeve JH, Saccenti E, Bouwman J, Dane A, Strassburg K, Vervoort J, Hankemeier T, Astrup A, Smilde AK, van Ommen B, et al. Weight loss predictability by plasma metabolic signatures in adults with obesity and morbid obesity of the DiOGenes study. Obesity (Silver Spring) 2016;24(2):379-88. doi: 10.1002/oby.21361.
- 15. Haufe S, Engeli S, Kaminski J, Witt H, Rein D, Kamlage B, Utz W, Fuhrmann JC, Haas V, Mahler A, et al. Branched-chain amino acid catabolism rather than amino acids plasma concentrations is associated with diet-induced changes in insulin resistance in overweight to obese individuals. Nutr Metab Cardiovasc Dis 2017;27(10):858-64. doi: 10.1016/j.numecd.2017.07.001.
- 16. Canfora EE, van der Beek CM, Hermes GDA, Goossens GH, Jocken JWE, Holst JJ, van Eijk HM, Venema K, Smidt H, Zoetendal EG, et al. Supplementation of Diet With Galacto-oligosaccharides Increases Bifidobacteria, but Not Insulin Sensitivity, in Obese Prediabetic Individuals. Gastroenterology 2017;153(1):87-97.e3. doi: 10.1053/j.gastro.2017.03.051.
- 17. Tremaroli V, Karlsson F, Werling M, Stahlman M, Kovatcheva-Datchary P, Olbers T, Fandriks L, le Roux CW, Nielsen J, Backhed F. Roux-en-Y Gastric Bypass and Vertical Banded Gastroplasty Induce Long-Term Changes on the Human Gut Microbiome Contributing to Fat Mass Regulation. Cell Metab 2015;22(2):228-38. doi: 10.1016/j.cmet.2015.07.009.
- 18. Johnston CS, Tjonn SL, Swan PD, White A, Hutchins H, Sears B. Ketogenic low-carbohydrate diets have no metabolic advantage over nonketogenic low-carbohydrate diets. Am J Clin Nutr 2006;83(5):1055-61.
- 19. Daud NM, Ismail NA, Thomas EL, Fitzpatrick JA, Bell JD, Swann JR, Costabile A, Childs CE, Pedersen C, Goldstone AP, et al. The impact of oligofructose on stimulation of gut hormones, appetite regulation and adiposity. Obesity (Silver Spring) 2014;22(6):1430-8. doi: 10.1002/oby.20754.
- 20. Zheng H, Lorenzen JK, Astrup A, Larsen LH, Yde CC, Clausen MR, Bertram HC. Metabolic Effects of a 24-Week Energy-Restricted Intervention Combined with Low or High Dairy Intake in Overweight Women: An NMR-Based Metabolomics Investigation. Nutrients 2016;8(3):108. doi: 10.3390/nu8030108.
- 21. Kamphuis MM, Lejeune MP, Saris WH, Westerterp-Plantenga MS. The effect of conjugated linoleic acid supplementation after weight loss on body weight regain, body composition, and resting metabolic rate in overweight subjects. Int J Obes Relat Metab Disord 2003;27(7):840-7. doi: 10.1038/sj.ijo.0802304.
- 22. Olli K, Salli K, Alhoniemi E, Saarinen M, Ibarra A, Vasankari T, Rautonen N, Tiihonen K. Postprandial effects of polydextrose on satiety hormone responses and subjective feelings of appetite in obese participants. Nutr J 2015;14(1). doi: 10.1186/1475-2891-14-2.
- 23. Khakimov B, Poulsen S, Savorani F, Acar E, Gürdeniz G, Larsen T, Astrup A, Dragsted L, Engelsen S. New Nordic Diet versus Average Danish Diet: a Randomized Controlled Trial Revealed Healthy Long-Term Effects of the New Nordic Diet by GC-MS Blood Plasma Metabolomics. J Proteome Res, 2016:1939-54.
- 24. Patil DP, Dhotre DP, Chavan SG, Sultan A, Jain DS, Lanjekar VB, Gangawani J, Shah PS, Todkar JS, Shah S, et al. Molecular analysis of gut microbiota in obesity among Indian individuals. J Biosci 2012;37(4):647-57.
- 25. Kunesova M, Braunerova R, Hlavaty P, Tvrzicka E, Stankova B, Skrha J, Hilgertova J, Hill M, Kopecky J, Wagenknecht M, et al. The influence of n-3 polyunsaturated fatty acids and very low calorie diet during a short-term weight reducing regimen on weight loss and serum fatty acid composition in severely obese women. Physiol Res 2006;55(1):63-72.

- 26. Lewis S, Wallin J, Kane J, Gerich J. Effect of diet composition on metabolic adaptations to hypocaloric nutrition: comparison of high carbohydrate and high fat isocaloric diets. Am J Clin Nutr 1977;30(2):160-70.
- 27. Meckling KA, O'Sullivan C, Saari D. Comparison of a low-fat diet to a low-carbohydrate diet on weight loss, body composition, and risk factors for diabetes and cardiovascular disease in free-living, overweight men and women. J Clin Endocrinol Metab 2004;89(6):2717-23. doi: 10.1210/jc.2003-031606.
- 28. Remely M, Tesar I, Hippe B, Gnauer S, Rust P, Haslberger AG. Gut microbiota composition correlates with changes in body fat content due to weight loss. Benef Microbes 2015;6(4):431-9. doi: 10.3920/bm2014.0104.
- 29. Yang MU, Barbosa-Saldivar JL, Pi-Sunyer FX, Van Itallie TB. Metabolic effects of substituting carbohydrate for protein in a low-calorie diet: a prolonged study in obese patients. Int J Obes 1981;5(3):231-6.